Primary Carcinoma of the Gallbladder

Review of 173 Cases

L. J. TRAGERMAN, M.D., Los Angeles

• *One hundred seventy-three cases of primary carcinoma of the gallbladder were analyzed. In the group studied they made 2.11 per cent of all malignant tumors found at autopsy and were found in 1.89 per cent of all cases in which operation was done on the biliary tract. There was no appreciable change in the incidence of this tumor at autopsy during the period studied (1918-1948) at the Los Angeles County Hospital. Sixty-eight per cent of the cases were in females. A particularly high incidence was noted in Mexican females.*

Upper abdominal pain, loss of weight, nausea and vomiting, jaundice, and palpable mass or enlarged liver were the most common clinical features. Approximately one-third of the patients in whom the lesion was found at operation and one-fifth of all the patients whose records were studied had a history of chronic gallbladder disease.

All but two of the 38 patients operated on were dead or had clinical recurrence within two years. One was alive and well 12 years after cholecystectomy.

The most common gross appearance, particularly at autopsy, was a large tumor mass replacing the gallbladder and radiating to nearby organs, particularly the liver. In about one-third of the cases the tumor was grossly limited to the gallbladder. Polypoid tumors occurred in only about 10 per cent of the cases and most of the tumors were diffusely growing adenocarcinoma. Perforation appeared in nine cases, usually with fistula to the gastrointestinal tract. All of the tumors were histologically adenocarcinoma, usually of simple glandular structure. No purely squamous cell growth occurred.

Gallstones were found in 79.8 per cent of the cases.

INTEREST IN PRIMARY CARCINOMA of the gallbladder is dulled by the relative infrequency of the disease and even more because it is generally recognized to be almost incurable. Five-year cures, such as that reported by Booher and Pack,[2] are rare indeed. Finney and Johnson[6] declare, "In many ways it seems hardly worth while to offer a paper on such a surgically hopeless condition as carcinoma of the gallbladder."

This gloomy situation has discouraged reports on this disease but has, on the other hand, encouraged study and speculation in an effort to arrive at better clinical results. Of chief interest to surgeons and pathologists has been the relationship of carcinoma of the gallbladder to the occurrence of gallstones, which are considerably more common in carcinoma of the gallbladder than in the general population. The possible etiological significance of this fact has intrigued pathologists and other investigators. Surgeons have considered with interest but have not agreed on whether the danger of malignant change is in itself an indication for cholecystectomy in asymptomatic cholelithiasis.

This report is based on a review of 173 cases of primary carcinoma of the gallbladder. The sources are autopsy reports from 1918 to 1948 on file at the Los Angeles County Hospital and surgical pathology reports for the years 1939 through 1947 inclusive plus the year 1949. (The surgical pathology material for the year 1948 was not indexed and hence was omitted.)

The clinical records, autopsy protocols and slides were reviewed and analyzed for pertinent data on incidence, clinical features and pathological findings. A few cases were omitted because information was insufficient or because the diagnosis seemed doubtful after review of the exhibits.

It might be mentioned in passing that, except for metastatic carcinoma, only three other malignant tumors of the gallbladder were recorded at the Los Angeles County Hospital in the period covered by this report. One of these was a primary fibrosarcoma of the gallbladder which occurred in a calculous gallbladder and caused death by extensive metastases. The other two were instances of lymphosarcoma and reticulum cell sarcoma involving the gallbladder as part of a widespread disease.

From the Los Angeles County Hospital and the Department of Pathology, School of Medicine, University of Southern California.

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TABLE 1.—*Incidence of Carcinoma of the Gallbladder (173 Cases)*

	Autopsies	Carcinoma of Gallbladder: Cases	Carcinoma of Gallbladder: Per Cent of Autopsies	Carcinoma of Gallbladder: Per Cent of Malignant Tumors	Operations on Biliary Tract	Carcinoma of Gallbladder: Cases	Carcinoma of Gallbladder: Per Cent
Los Angeles County Hospital....	38,757	135	0.35	2.11 (all malignant tumors)	2,011	38	1.89
Collective Review of Literature by Arminski[1]	206,098	908	0.43	4.53 (carcinoma only)	46,480	569	1.22

TABLE 2.—*Comparative Incidence of Primary Carcinoma of the Gallbladder Found at Autopsy (Los Angeles County Hospital, 1918-1947)*

Years	Autopsies	Malignant Tumors Found	Per Cent of All Autopsies	Carcinoma, Gallbladder: Cases	Carcinoma, Gallbladder: Per Cent of All Tumors	Carcinoma, Pancreas: Cases	Carcinoma, Pancreas: Per Cent of All Tumors	Carcinoma, Lung: Cases	Carcinoma, Lung: Per Cent of All Tumors
1918-22	1,176	132	11.2	3	2.3	9	6.8	0	0
1923-27	3,496	493	14.1	10	2.0	22	4.5	21	4.3
1928-32	5,055	659	13.0	14	2.1	28	4.2	29	4.4
1933-37	9,647	1,433	14.8	31	2.2	58	4.0	83	5.8
1938-42	10,741	1,908	17.8	43	2.3	98	5.1	212	11.1
1943-47	8,632	1,759	20.4	34	1.9	68*	4.9	158*	11.3
Total	38,757	6,384	16.5	135	2.1	283	4.7	503	8.4

*4 years only (1943-46).

No attempt to review the literature was made in connection with this report. An excellent collective review was published by Arminski[1] in 1949. He reviewed reports of 908 cases among 206,098 autopsies reported in the world literature from 1894 to 1940, and 569 cases among 46,480 operations on the biliary tract from 1891 to 1941. He added reports of 25 cases he had observed. Since then (up to February 1952) there have been seven additional reports in the American literature, reporting 193 additional cases.

INCIDENCE

Data on 135 of the 173 cases covered in this review were obtained from the autopsy reports. Those cases made up 2.11 per cent of the total number of malignant tumors found at autopsy during the 25-year period covered. The other 38 cases of primary carcinoma of the gallbladder were studied in the surgical pathology laboratory during a ten-year period. They made up 1.89 per cent of all cases in which operation was done on the biliary tract and 2.8 per cent of all cases in which cholecystectomy was carried out. The incidence observed in autopsy reports (Table 1) was considerably lower than that reported by Arminski.[1]

The records of all cases of malignant tumor in which autopsy was done at the Los Angeles County Hospital from 1918 to 1947 were analyzed recently by Steiner, whose findings, both published and unpublished, have been freely drawn upon in preparing this report. The author is indebted to him for basic data essential to study of incidence and for specific observations regarding carcinoma of the gallbladder.

The quinquennial incidence of primary carcinoma of the gallbladder as observed at autopsy at the Los Angeles County Hospital for the period studied is shown in Table 2. It is compared with the findings of Steiner, Butt, and Edmondson[11] at the same hospital for the incidence of all malignant tumors, primary carcinoma of the lung and carcinoma of the pancreas, their figures being modified slightly to include 1947. Carcinoma of the lung is included for purposes of comparison as a tumor of increasing incidence, and carcinoma of the pancreas as a tumor which has not increased in incidence and which is clinically related to primary carcinoma of the gallbladder. This table indicates a fairly constant incidence of the disease during the period studied.

Steiner in his review of malignant tumors found at autopsy at the Los Angeles County Hospital tabulated all of the cases according to sex and race. Most patients at the Los Angeles County Hospital are of the Caucasoid, Mexican and Negroid races, 98.8 per cent of all autopsies being done in these races. Mexicans are listed separately because so large a proportion (17.4 per cent) of all autopsies at this hospital were done on persons of that race.

In analyzing the age, sex, and racial distribution for cases of primary carcinoma of the gallbladder seen at autopsy, Steiner found a notably higher rate in Mexican females than in any other group: While the corrected sex ratio of 2.88 females to 1 male reflected the known predisposition of females to this disease, the incidence in Mexican females was almost three times that in Caucasoid females. He also noted that the peak of incidence was at a lower age in Mexican than in Caucasoid females.

The distribution by age, sex, and race for the 173 cases recorded in autopsy reports and in surgical pathology reports is shown in Table 3. Of these, 118 or 68.2 per cent were in females, a proportion close to the 73.1 per cent in females reported by Arminski.[1] Table 3 also illustrates that the disease occurs more frequently in younger persons among Mexicans than among Caucasoids. Four of the seven patients under 40 years of age were Mexican females. The sex and racial distribution of the 173 cases compared with the percentage distribution of the same groups in 35,293 autopsies was as follows:

Race-Sex Group	Percentage of All Cases of Carcinoma of Gallbladder	Percentage of All Autopsies (35,293)
Caucasoid male	27.2	48.1
Caucasoid female	42.8	27.0
Mexican male	3.5	9.4
Mexican female	21.9	8.0
Negroid male	1.2	3.4
Negroid female	3.5	2.9

The unusually high incidence in Mexican females is further illustrated by the fact that carcinoma of the gallbladder comprises over 8 per cent of all malignant tumors found at autopsy in Mexican females.

CLINICAL FEATURES

Symptoms and Physical Findings

The incidence of the most common symptoms and signs in the 173 cases is shown in Table 4. Percentages are based on cases in which definite information was available. The findings are similar to those reported in the literature.

Abdominal pain when present was usually in the right upper quadrant of the abdomen and was of the colicky type in 21 per cent of the surgical pathology cases and 9.3 per cent of all the cases. The pain was variously described as dull, sharp, intermittent or continuous. Radiation to the back or right shoulder was present in some cases. The duration of pain in the surgical pathology group varied from one week to over ten years. Abdominal tenderness was present in many cases, particularly in the surgical group.

History suggestive of chronic gallbladder disease was reported for 34 per cent of the surgical group and for 22 per cent of all cases. In the collective review of Arminski[1] the incidence of past history of gallbladder disease was 52 per cent.

Weight loss, frequently rapid and pronounced, occurred in almost all cases, even those in which patients were still obese when admitted to the hospital.

Jaundice was present in 28 of the 38 surgical cases and in 108 of the 160 cases in which definite information was available. In the surgical group one patient had had jaundice for eight months at the time of operation, but in no other case had jaundice been present for more than four weeks before operation.

TABLE 3.—*Age, Sex, and Race Distribution of 173 Cases of Carcinoma of the Gallbladder*

Age	Caucasoid Male	Caucasoid Female	Mexican Male	Mexican Female	Negro Male	Negro Female
21-30	..	1	..	..	..	..
31-40	..	..	1	4	..	1
41-50	3	3	2	9	..	..
51-60	9	16	1	11	1	2
61-70	13	27	1	10	..	2
71-80	17	21	1	3	..	1
81-90	5	6	..	1	1	..
Total	47	74	6	38	2	6

TABLE 4.—*Incidence of the Most Common Symptoms and Signs in 173 Cases of Carcinoma of the Gallbladder*

Symptom or Sign	Surgical Cases No.	Surgical Cases Per Cent	All Cases No.	All Cases Per Cent	Percentage in Collective Review by Arminski[1]
Pain in abdomen	33	86.8	110	73.3	76.1
Weight loss	17	94.4	87	66.5	64.1
Nausea or vomiting	22	81.5	81	67.5	.....
Jaundice	28	73.7	108	67.5	57.7
Mass in right upper quadrant	18	58.1	76	55.9	53.2
Enlargement of liver	22	68.8	99	71.7	49.1
Tenderness	20	90.9	79	62.2	64.0
Ascites	0	0	27	20.1	20.8

Pain occurring at some time during the course of the disease was associated with jaundice in almost all cases. Painless jaundice occurred in only four of the surgical cases and in 18 of all cases.

Enlargement of the liver or a palpable mass in the upper abdomen was noted in well over half the cases. Frequently it was difficult to differentiate between a mass and an enlarged liver.

Laboratory and Roentgenographic Findings

Erythrocyte counts or hemoglobin determinations were made in 21 of the surgical cases. In eight there was no anemia; in five anemia was slight, and in seven moderate. Data available on 76 of the 135 cases in the autopsy series disclosed no anemia in 16, slight in 12, moderate in 32 and severe in 18. Most of the other laboratory studies were concerned with differential diagnosis of jaundice or evaluation of liver function. A wide range of results was recorded which do not seem statistically valuable in this study.

Because of the tendency of carcinoma of the gallbladder to destroy this organ and to form a large local mass centering about the gallbladder, and because of the frequent presence of gallstones, a high incidence of roentgenographically observable abnormalities would be expected. Cholecystograms made in 25 cases within a reasonably short time before operation or autopsy showed the gallbladder to be nonfunctioning in 24 cases and to contain stone in 8; in 2 cases examination was unsatisfactory but in no case were the findings reported as normal. In

most cases with nonfunctioning gallbladder the tumor involvement of the gallbladder was extensive, but in no case was the tumor visualized or outlined by roentgenographic appearance. A plain film of the gallbladder was made in 23 cases. In eight cases stones only were observed, in three cases a mass only, and in two both mass and stones. In ten cases no abnormality was visualized in the plain film, although at autopsy stones were found in eight cases and in several there were tumors large enough to extend beyond the gallbladder. In roentgenographic studies of the gastrointestinal tract abnormalities resulting from pressure or invasion by tumor were frequently observed. These were late findings but in some cases were helpful in diagnosis, while in others they were misinterpreted as indicating that the gastrointestinal tract was the site of the primary tumor. The change most frequently present was duodenal deformity; other frequent findings were abnormalities in the stomach and large bowel. Cholecystoduodenal fistula was observed in only one case.

In a number of the reports in the literature cases have been classified according to the dominant or composite clinical impression, a more graphic presentation than tabulation of symptoms and signs. The cases in this study have been considered in this way, by a classification modified from Boyce and McFetridge:[3]

a. Cases with recent symptoms and signs of gallbladder disease, but with no evidence to suggest malignant disease 13

b. Cases with past and recent symptoms and signs of gallbladder disease with no evidence to suggest malignant disease 11

c. Cases with recent history of gallbladder disease and recent symptoms and signs of malignant disease..... 34

d. Cases with past symptoms and signs of gallbladder disease and evidence of malignant disease..... 24

e. Cases with evident malignant change and no symptoms or signs of gallbladder disease..... 47

f. Cases with no evidence of malignant or gallbladder disease 14

g. Cases with obstructive jaundice as principal clinical feature 17
- Painless jaundice 8
- With pain, usually in right upper quadrant, and often a mass..... 9

(Jaundice was also present in 19 additional cases in Groups *a* and *d*.)

h. Cases in which information was inadequate..... 13

Only 35 patients had a history of chronic gallbladder disease while 60 patients had no symptoms of gallbladder disease.

Clinical Diagnosis and Course

The clinical diagnoses made in the 38 cases in the surgical group were as follows: Cholecystitis or cholelithiasis, 10; obstructive jaundice, 10; carcinoma of the pancreas, 6; carcinoma, site not specified, 4; carcinoma of the bowel, 3; carcinoma of the gallbladder, 3; hepatitis, 2.

The most common diagnosis in the 135 cases in the autopsy group was that of intra-abdominal malignant disease, made in 75 cases—carcinoma of the stomach in 20, of the pancreas in 16, and of the gallbladder in 13.

The correct diagnosis was made before operation or autopsy in only 16 of the 173 cases, a proportion similar to that reported in the literature. There was no constant clinical pattern in these cases. There was a definite history of gallbladder disease in five cases and of painful jaundice and a palpable mass in several. Correct diagnosis was made before operation in three patients. One of them was a Negro woman 62 years of age who entered the hospital because of constant pain, a mass in the right flank, and loss of weight. She had had gallbladder drainage for stones three years previously. The second was an obese Mexican woman 60 years old who was admitted to the hospital in an attack of colicky pain in the right upper quadrant of the abdomen and a palpable mass; she had had chronic cholecystitis with intermittent colic for fifteen years. The third patient was a 73-year-old white woman who for a short time had had jaundice and pain in the area of the gallbladder, radiating to the shoulder, and a palpable firm mass in the right upper quadrant of the abdomen.

It is noteworthy that pain was present in five of the six surgical cases diagnosed before operation as carcinoma of the pancreas and in all ten cases diagnosed before operation as obstructive jaundice.

In the autopsy group symptoms preceded death by less than a year in 60 cases, and operation was attempted in only 20, in 14 of which the tumor was inoperable and death ensued within a year. In one patient extensive resection of the gallbladder, duodenum and colon was done; the patient died of postoperative shock and widespread metastases were found at autopsy. Cholecystectomy was done on four patients, two of whom died in the immediate postoperative period, one with metastases which were found at autopsy. The other two died of metastases in four weeks and in 17 months respectively.

The clinical course of the 38 surgical cases was equally poor:

Duration of Symptoms	Cases	Cases with Metastases Found at Operation
Less than 1 month	12	9
1 to 6 months	17	15
12 to 18 months	3	3
18 to 24 months	1	1
2 to 5 years	3	1
Unknown	2	0

The operative procedures done in these patients were: cholecystectomy (23); cholecystostomy and biopsy (2); exploration and biopsy (11); cholecystoduodenostomy and biopsy (1); cholecystogastrostomy and biopsy (1).

TABLE 5.—*Incidence of Gallstones in 173 Cases of Carcinoma of the Gallbladder*

Age	Number of Cases	Number with Gallstones	Per Cent with Gallstones	Location of Stones: Gallbladder	Cystic Duct	Hepatic Ducts	Common Bile Duct
21-30	1	1	100.0	1	0	0	0
31-40	6	4	66.6	4	0	0	1
41-50	17	13	76.4	13	1	0	0
51-60	40	34	85.0	33	4	0	4
61-70	53	44	83.0	42	5	1	8
71-80	43	33	76.7	30	2	0	8
81-90	13	9	69.2	9	1	0	1
Total	173	138	79.8	132	13	1	22

The known postoperative survival of this group was as follows:

Operative deaths	4	(3 with metastases)
Less than one month	6	(all died)
1 to 6 months	15	(all with metastases; 11 died)
6 months to 1 year	4	(3 with metastases; 2 died; 1 living and well, no further follow-up)
1 to 2 years	6	(5 with metastases; 3 died; 1 living and well, no further follow-up)
2 to 5 years	0	
Over 5 years	1	(last seen Nov. 1951 5 years and 3 months after operation; had lost 30 pounds of weight, and has many cardiac and gastrointestinal complaints)
Over 10 years	1	(alive and well 12 years after operation)
Unknown	1	

Thus of all patients followed all but three were dead or had recurrence within two years and only two were known to be alive after five years. One of these, the youngest in the group, was 24 years old at the time of operation and is in good health after twelve years. Her symptoms and the findings were those of acute cholecystitis and the tumor was found unexpectedly.

PATHOLOGICAL ANATOMY

Gross Pathology

There are several important components of the gross pathologic changes relative to carcinoma of the gallbladder. These are the appearance of the tumor itself, the changes produced in the gallbladder by the tumor or from preexisting disease, and the nature of the extension and metastases.

In almost all instances the disease was far advanced at the time of operation or autopsy. Examples of early lesions were rare. There were only eight cases in which the tumor was not observed until microscopic study was carried out; in those cases the growth was limited to the mucosa or wall of the gallbladder. Even in those cases, with one exception, the disease had already metastasized and later caused death. In a few instances the tumor was limited to one portion of the wall of the gallbladder, producing a nodule, plaque or small polypoid tumor. In most instances the growth filled the lumen (except for stones) or replaced the wall, frequently with direct extension into adjacent structures, particularly the liver. Polypoid tumors occurred in only 21 of the 173 cases.

The tumor was grossly limited to the gallbladder in 62 cases, the gallbladder being shrunken and contracted in 23 cases, of normal size in 29, and distended or enlarged in 19.

Most frequently the gross appearance was that of wide local growth radiating from the gallbladder into the nearby organs, particularly the liver. Such a large local tumor was present in this series in 106 cases, in most of which the gallbladder was itself small or normal in size; it was enlarged or distended in only 12 cases. In 32 cases the gallbladder was destroyed by tumor; often only remnants remained within the mass, identifiable only by the cluster of stones frequently present. The formation of a large local mass was frequently detectable by physical examination and in some cases by roentgenographic studies.

Perforation occurred in nine cases. In six of them a fistula was formed to the gastrointestinal tract, and in three there was generalized peritonitis (bile peritonitis in one case). In two cases local abscesses were present.

The bile ducts were involved by direct extension in 81 cases (47 per cent), the common bile duct in 44 of these. In some cases the growth followed the bile ducts and could be distinguished from primary carcinoma of extrahepatic bile ducts only with difficulty if at all.

In addition to the local mass in the liver there were disseminated metastatic nodules in 80 cases. Regional lymph node metastases were described in 84 cases (49 per cent). Less frequently involved in metastases were the peritoneum (43 cases), the gastrointestinal tract (41), the pancreas (23), lungs (10), bones (6), kidneys (6), adrenal glands (6), the portal vein (6), the superior vena cava (2), ovaries (5), pleura (5), abdominal wall (3), diaphragm (3), spleen (2), pericardium (1), and myocardium (1).

The most common associated pathologic condition was gallstones, which occurred in 138 or 79.8 per cent of the cases (Table 5). Stones were also present in the bile ducts in 36 cases, in the common bile duct in 22. As the disease was usually in a late stage when observed and the organs diffusely infiltrated, it was difficult and often impossible to find gross evidence of preexisting cholecystitis. Hydrops or empyema of the gallbladder was present in only three cases.

Other associated diseases were abscess of the liver or suppurative cholangitis (five cases), double primary carcinoma (six cases — two of the prostate, two of the uterus, one of the colon, and one of the ovary) and diabetes (six cases).

There were only six cases in which carcinoma of the gallbladder was an incidental finding and not a major cause of death.

Microscopic Pathology

All the tumors in the series were adenocarcinomas. The histological types were as follows:

Simple glandular adenocarcinoma		110
Undifferentiated adenocarcinoma		24
Anaplastic carcinoma	19	
Carcinoma simplex	5	
Colloid (mucoid) carcinoma		5
Scirrhous carcinoma		4
Papillary carcinoma		2
Mixed types of adenocarcinoma		22
Mixed squamous and adenocarcinoma		6

There were no cases of pure squamous cell carcinoma in the series. The most common histologic type was simple glandular carcinoma infrequently having a slight resemblance to gallbladder epithelium. More often the cellular structure resembled that of carcinoma of the gastrointestinal tract. There were no early lesions which could be studied for histogenesis. In the few cases in which involvement could be observed only microscopically the tumor was fairly advanced. In two cases the appearance of the tumor was suggestive of carcinoma in situ; in both the tumor was in the mucosa and in the epithelium of the Rokitansky-Aschoff sinuses. No epithelial metaplasia was seen in uninvolved epithelium.

In most cases the widespread tumor growth in the wall of the gallbladder had obliterated any evidence of preexisting chronic cholecystitis. However, in almost all cases where portions of wall were still present and uninvolved by tumor, chronic inflammatory changes including fibrosis were present.

RELATIONSHIP TO CHRONIC CHOLECYSTITIS AND CHOLELITHIASIS

It is generally held that chronic cholecystitis precedes carcinoma of the gallbladder in most cases. There was little opportunity to study this relationship in this series because the disease was advanced in most cases. However, in most instances where it could be studied there was evidence of chronic inflammation or fibrosis, although histogenesis and the preexistence of nonmalignant alterations in the epithelium could be observed in only a few cases. In two cases histological findings suggested adenoma malignum or carcinoma in situ. In many of the cases in which malignant growth was far advanced, areas of uninvolved mucosa could be found, and in these areas the epithelium was normal.

Cholelithiasis was present in 138 or 79.8 per cent of the 173 cases (Table 5). Arminski[1] reported an incidence of 73 per cent in his collective review of the literature. Most observers believe that the stones, like the inflammatory changes, antedate the tumors, and some have suggested that the stones are an important causative factor. This has led to attempts at production of carcinoma of the gallbladder in experimental animals, usually guinea pigs, by placing human gallstones and other substances within the gallbladder. Desforges and co-workers[5] in a recent report indicated that the results, particularly with gallstones, were either negative or inconclusive.

It is well known that gallstones occur more frequently in females than in males. Data on age and race differences are not as abundant but in general the incidence increases with age in both sexes and is lower in the Negroid than in the Caucasoid races. Among persons with carcinoma of the gallbladder the incidence of stones is greater than in the general population and is also greater proportionately for males and for Negroid persons. This incidence suggests that if gallstone antedates the development of carcinoma it may be a predisposing factor, although it must be remembered that gallstones are quite common, particularly in older persons, while carcinoma of the gallbladder is rare.

If gallstones are in some way related to the development of carcinoma of the gallbladder, some parallelism in age, sex, and racial distribution of the two conditions might be expected, although this incidence may, of course, be purely coincidental, as in the increase of incidence with age. According to available statistics, as in the recent report of Lieber,[9] the incidence of gallstones is highest in Caucasian females and lowest in Negro males. Similar variations are to be noted in data on carcinoma of the gallbladder. According to figures from the Los Angeles County Hospital for the period 1918 to 1937, the incidence of gallstones found at autopsy was 4.4 per cent, but no breakdown as to age, sex, race or fatal outcome is available for the period covered by this report. For the years 1934 through 1937, the incidence of gallstones in 8,158 autopsies on persons

over 10 years of age was 6.3 per cent. Distribution by race and sex was as follows:

Race	Per Cent of All Autopsies	
	Male	Female
Caucasoid	4.7	8.6
Mexican	3.8	9.8
Negroid	3.6	4.1

Although the incidence of gallstones is greater in females than in males, with the greatest sex difference in the Mexican race, there is only a slightly greater incidence of stones in Mexican females than in Caucasoid females. Among younger females, however, the racial difference is greater: In 19,908 autopsies the incidence of gallstones in Mexican females under 40 years of age was 29 per cent, while in Caucasoid women of the same age the incidence was only 8 per cent.

As previously mentioned, the very poor results of treatment for carcinoma of the gallbladder have led some observers to advocate prophylactic cholecystectomy in any patient who has gallstones, even if there are no symptoms. Others point out that gallstones are so common in middle age and later life and the incidence of carcinoma of the gallbladder so low that the operation would entail a greater risk than the disease. Some of the differences of opinion arise from variations in reported incidence of gallstone and, to a lesser extent, of carcinoma of the gallbladder, particularly in reports based on examination of surgical specimens.

It is of little or no value to quote statistics on average or total incidence of gallstones because of the wide variations in sex and race. Reports of large series of cases analyzed by age, sex, and race, as in the recent excellent report by Lieber,[9] are needed. Comparable statistics on carcinoma of the gallbladder are also needed but are difficult to obtain in large numbers. Additional studies of experimentally induced tumors of the gallbladder, as well as histological studies of early lesions, should also be of value in the problem of the relationship of cholelithiasis to carcinoma of the gallbladder.

673 South Westlake Avenue.

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